

REMARKS/ARGUMENTS

In this response, Claims 2-5 have been added. The subject matter contained in the newly-added claims are fully supported by the disclosure in the application and are not disclosed or taught by the prior art. Thus, Claims 1-5 remain pending in the present application.

I. Specification

Examiner acknowledges the substitute specification comprising the amendments as suggested by Examiner in the previous Office Action. Examiner, however, states that the substitute specification could not be entered because an accompanying clean version (without markings) and a statement that the substitute specification contains no new matter was not provided.

Applicant submits herewith a clean version of the specification without any markings. No new matter has been added by the amendments contained in the substitute specification.

II. Claim Rejections - 35 U.S.C. § 103(a)

Claim 1 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Mashberg et al., A Cancer Journal for Clinicians, Vol. 45, No. 6, pages 328-351, Nov-Dec 1995, ("Mashberg") in view of Rosin et al., Clinical Cancer Research, Vol. 6, pages 357-362, Feb 2000 ("Rosin"). Applicant respectfully disagrees.

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. M.P.E.P. 2134.01. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

The Examiner states that Mashberg does not teach "extracting DNA from the resected tissues and examining the DNA for allelic losses for mutations of tumor suppressor genes." Office Action, dated 7/14/2006, at page 4. The Examiner then states that "Rosin provides the limitations not found in the Mashberg reference and provides motivation for performing further analysis on biopsy tissue samples." *Id.* at page 5.

There is no teaching, suggestion, or motivation to combine or modify the teachings of Mashberg and Rosin to produce the claimed invention. Applicant's claimed invention is directed to providing a "prognostic method for the early prediction of eventual development of invasive epithelial cancer" on epithelial tissue. In contrast, Mashberg addresses the diagnosis of oral and oropharyngeal cancers. The difference is that Applicant's claimed invention provides a method for predicting whether epithelial cancer is likely to develop in the future and Mashberg

discloses methods for diagnosing a cancerous condition that is already in existence in its early stages. In other words, Applicant's claimed invention provides a prognosis, whereas Mashberg provides a diagnosis.

Applicant's claimed invention is based on the surprising and unexpected discovery that toluidine blue stains not only cancerous tissue, but also precancerous tissue, and further that such precancerous tissue may provide "the earliest indications of genetic alterations which are precursors to the development of invasive cancer." Specification, at page 11.

In contrast, Mashberg does not disclose, teach or suggest that toluidine blue may be used to locate precancerous or clonal tissue. Instead, Mashberg would interpret such a result as a "false positive" as Mashberg teaches that "[t]oluidine blue clinically stains malignant lesions, but not normal mucosa." Mashberg, at page 345-347.

Applicant therefore has discovered that toluidine blue may be used to identify tissues that may be subjected to further genetic analysis: "This molecular analysis definitively shows that approximately 80% of the lesions identified by the Mashberg-type protocol are clonal." Specification, at page 17. Applicant further states that "preneoplastic changes identified by the toluidine blue dye in this patient population are clonal and are therefore in the progression pathway to cancer." Specification, at page 18-19.

There would be no motivation to combine Mashberg with Rosin, as the disclosure in Mashberg is limited to providing a diagnosis of oral and oropharyngeal cancers and does not teach the prognostic method for the future development of epithelial cancer that is described and claimed by Applicant.

Therefore, because there is no teaching, suggestion, or motivation to combine Mashberg and Rosin, and because of the demonstrated surprising and unexpected results from the claimed methods, Applicant respectfully requests that the rejection under § 103 should be withdrawn. Reconsideration and withdrawal of the rejection is respectfully requested.

III. Claim Rejections - 35 U.S.C. § 112: New Matter.

Claim 1 is rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner states:

The amendment to the claim to recite "epithelial cancer" was not found anywhere in the specification as filed. The specification teaches in the Examples that the method relates to head and neck cancer (page 16). While the specification teaches the use of epithelial tissue in the staining analysis method, the specification makes no reference to any epithelial cancer, which broadly encompasses numerous cancer types (e.g., breast, prostate, colon, and etc) that are not adequately described or disclosed. Thus, the specification does not provide support for the invention as currently claimed.

Office Action, dated 7/14/06, at page 7. Applicant respectfully disagrees.

The fact that the precise wording "epithelial cancer" is not found in the specification does not mean that the specification does not provide support for the invention as currently claimed. The written description requirement does not require that the claims utilize the same language as contained in the specification. See MPEP § 2163 ("there is no *in haec verba* requirement" for newly added claims). What is required by the written description requirement is that the added claim limitations be "supported in the specification through express, implicit, or inherent disclosure." Id.

In fact, Examiner acknowledges that "the specification teaches the use of epithelial tissue in the staining analysis method." Id. Additional support is provided in the specification, where the Applicant specifically describes Mashberg as providing an *in vivo* diagnostic screening test that "identifies and delineates suspect sites on epithelial tissue." Specification, at ¶ [0012].

Because the claimed invention is based on identifying clonal patches of epithelial tissue by applying a staining dye that is selectively retained by mitochondria of neoplastic and preneoplastic cells of the epithelia, it supports the claimed prognostic method as it relates to cancer in the epithelial tissue or "epithelial tissue." The fact that the specification discloses the Examples in connection with epithelial tissue that is located in the head and neck area does not, and cannot, limit the scope of the claimed invention.

The specification and Claim 1, as originally filed, broadly recited the method in connection with "invasive cancer." Accordingly, there is nothing in the Specification or the originally-filed claim that limits the practice of the claimed method to "head and neck cancer." Applicant's subsequent amendment to Claim 1 narrowed the scope to "invasive epithelial cancer" to more precisely recite the types of tissue.

The specific Examples describing the method as it relates to head and neck cancer should not operate to limit the scope of the claims, as the Specification expressly states, in the paragraph preceding the Examples, that:

The following examples are provided to illustrate to those skilled in the art the practice of my invention and the presently preferred embodiments thereof. These examples are not to be understood as limiting the scope of the invention, which is defined only in the appended claims.

Specification, at ¶ [0034].

In view of the foregoing, Applicant respectfully requests that the rejection of Claim 1 under 35 U.S.C. § 112, first paragraph, be withdrawn.

CONCLUSION

It is believed that all claims now pending patentably define the subject invention over the prior art and are in condition for allowance. Applicants respectfully request that the claims be allowed and earnestly solicit favorable action at the earliest possible date.

Applicant also requests to schedule a telephone interview with the Examiner to discuss the issues raised in the Final Office Action, dated July 14, 2006, and Applicant's claim amendments and arguments in response thereto.

If any additional fees are due in this matter, please charge our Deposit Account No. 10-0440.

Respectfully submitted,

JEFFER, MANEELS, BUTLER & MARMARO LLP

Dated: January 12, 2007

By: 

Rod S. Berman, Esq.
Reg. No. 31,483
1900 Avenue of the Stars
Seventh Floor
Los Angeles, CA 90067-4308
(310) 203-8080